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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,080	10/08/2004	J. Phillip Bowen	B40-002	3420

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EXAMINER	
GULLEDGE, BRIAN M	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
10/28/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,080	BOWEN ET AL.	
	Examiner	Art Unit	
	Brian Gulledge	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,50-56 and 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40,50-56 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/28/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Previous Rejections

Applicants' arguments, filed 4 October 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement filed 28 September 2010 fails to comply with 37 CFR 1.97(c) because it lacks the fee set forth in 37 CFR 1.17(p) or a statement as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered.

Claim Amendment

The claim amendment received 4 October 2010 is acknowledged. The claim amendment reinstates previously cancelled claim 66. This is not proper, as a "claim which was previously canceled may be reinstated only by adding the claim as a "new" claim with a new claim number." See 37 CFR 1.121(c)(5). However, in the interest of compact prosecution, the subject matter claimed in claim 66 will be considered.

Claim Objections

The objection of claim 50 under 37 CFR 1.75(c) is maintained, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim repeats the identical options for the tumor that are recited by instant claim 40, and does not further limit the claim. Applicant argues that claim 50 does recite fewer tumors than claim 40, and thus the objection is not proper. However, both claims 40 and 50 recite three and only three options for the tumors, which are the same in each instance, and claim 50 does not recite fewer tumors than claim 40.

Claim Rejections - 35 USC § 112, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40 and 51-56 stand rejected and claim 66 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Applicant argues that the rejection is not proper. The Applicant notes that based on the declaration submitted under 37 CFR 1.132 on 4 October 2010 the presently claimed invention is enabled and therefore, patentable. Applicant states that the claimed solenopsin compounds are inhibitors of phosphatidylinositol-3 kinase (referring to two cited references for support). Applicant further states by virtue of the effect these compounds have on both direct and indirect angiogenesis and the fact that angiogenesis is consistent with favorable therapeutic outcomes in a variety of cancers and tumors that the claimed invention will provide for a favorable therapeutic intervention in the treatment of a broad range of tumors and cancers.

The Examiner acknowledges both the arguments presented and the declaration submitted under 37 CFR 1.132, but does not consider them persuasive. As an initial matter, the Examiner notes that page 2 of the declaration is missing (including paragraphs 6-15). However, these missing paragraphs appear to be paragraphs detailing the background of the declarant, as the paragraphs preceding and following these paragraphs (paragraphs 3-5 and 16-25) also detail the background of the declarant.

The Applicant and declarant both state that the claimed solenopsin compounds are inhibitors of phosphatidylinositol-3 kinase. The Examiner notes that the two references cited (Park et al. and Arbiser et al.) in this discussion are not included with the response, and the Examiner is unable to determine the content of one of these two references (Park et al.). However, the other reference, the Arbiser et al. reference, was previously cited by the Office, and further this reference contradicts the statements put forth that the claimed solenopsin compounds

are inhibitors of phosphatidylinositol-3 kinase (PI3K). Arbiser et al. states that solenopsin inhibits the PI3K signaling pathway (abstract). However, Arbiser et al. also states that solenopsin "did *not* inhibit purified PI3K" (emphasis original; page 564, right column, lines 2-3). In view of this clear statement by Arbiser et al. and the lack of any evidence to the contrary, solenopsin is considered to not inhibit PI3K, contrary to the conclusion of the Applicant and the declarant.

The declarant also states that studies in the Folkman lab, published in the Proceedings of the National Academy, demonstrate that blockade of PI3K inhibits the growth of a tumor *in vivo*. No evidence is presented to support this conclusion. The data is not provided, the citation for this reference was not put forth, and a copy of the reference was not provided. No further discussion of the type of testing performed, tumors treated, or the compounds tested is provided.

The specification discloses that a dose of 3 μg/mL of one of the two enantiomers claimed inhibits cell growth of SVR cells, which are used to screen for angiogenesis inhibitors. The figure also shows that either a dose of 1 μg/mL or a dose of 6 μg/mL also inhibits cell growth of SVR cells. It is unclear which bars of the data presented correlate to each dose. The other dose has either no effect or stimulates growth, and it is unclear which due to the lack of error bars. The specification, however, provides no data regarding the use of the claimed compounds to treat tumors or cancers, either *in vitro* or *in vivo*.

The Applicant and declarant also state that favorable therapeutic outcomes in a variety of cancers and tumors would be expected by virtue of the anti-angiogenic effect these compounds have. The declarant refers to Arbiser et al. to support the conclusion that the claimed compound is a potent angiogenesis inhibitor in a zebrafish model. Arbiser et al. states that after 6 hours, it

appears that solenopsin may delay angiogenic precursors in the embryos (page 564, left column, lines 6-11). The Examiner does not consider this data sufficient to rebut the rejection. This data does not demonstrate the claimed compounds are useful for the treatment of any cancers or tumors.

Even if the data demonstrated that the compounds are anti-angiogenic, the subject matter claimed was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. To be enabling, the specification of the patent must teach those skilled in the art how to make and use the claimed invention without undue experimentation. As stated previously, the art is unpredictable. This conclusion is supported by previously cited Johnson et al. (*British Journal of Cancer*, **2001**, 84(10), pages 1424-1431), Voskoglou-Nomikos et al. (*Clinical Cancer Research*, **2003**, *9*, pages 4227-4239), and Suggitt et al. (*Clinical Cancer Research*, **2005**, *11*, pages 971-981).

For example, as stated previously, Voskoglou-Nomikos et al. states that their results suggest that the *in vitro* human tumor cell line and the human tumor xenograft models might have predictive value in some solid tumors (such as ovary and NSCLC) under both the disease and compound-oriented approaches, as long as an appropriate panel of tumors is used in preclinical testing (page 4237, left column, fourth paragraph). No data is provided by the declarant or Applicant for even one tumor. And Suggitt et al. concludes that while *in vitro* screening methods are useful in selecting compounds for secondary, more comprehensive, *in vivo* testing, they cannot reliably be used to predict in vivo activity. The gap between the presented *in vitro* testing of the claimed compounds for a antiangiogenic activity and PI3K pathway inhibition to treatment of a wide variety of cancers and tumors in human patients is not

accounted for by the data presented, and in view of the unpredictable nature of this art those skilled in the art would need to resort to undue experimentation in order to perform the claimed method.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 60 limits the cancer to cutaneous malignancy. Claim 40, from which this claim depends, limits the cancers to those selected from a particular list, but the species recited do not include cutaneous malignancy. Thus, claim 60 recites an option outside of the breadth of claim 40, and it is unclear which listing of cancers applies to the claimed method.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Gulledge whose telephone number is (571) 270-5756. The examiner can normally be reached on Monday-Thursday 6:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BMG

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612